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Craniofacial Fibrous Dysplasia: Surgical Management and Long-Term Outcomes at a Referral Center in Mexico City

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Abstract

Background Craniofacial fibrous dysplasia (CFD) is an uncommon benign condition in which a bone is replaced by fibrous tissue. An adequate clinical characterization considering the number of affected bones and functional impairment is important to determine the most effective surgical intervention for its management. This study aims to present our institution's experience in the evaluation and management of CFD.

Methods This was a retrospective study that included patients with CFD managed at our institution. Data included demographic characteristics, afflicted bones, surgical procedures performed, and recurrence. Results are presented as mean and percentages. Recurrence-free years and association between the type of surgery and recurrence was evaluated.

Results Eighteen patients were included (11 females, 61%). The zygomatic, maxillary, and frontal bones were the most commonly affected with eight (18%) cases each. The most common procedure was bone burring, with 36 procedures. Recurrence was more prevalent after burring (58.3%) and occurred earlier than in the bone resection group (13 vs. 15 years, $p > 0.05$).

Conclusion Surgery continues to be the cornerstone of CFD treatment. Bone burring is effective for debulking and contouring but increases the risk for recurrence. An individualized approach should be tailored according to the anatomical location of the disease, type of CFD, behavior of the lesion, and accompanying clinical complaints.

Keywords
- fibrous dysplasia
- polyostotic
- craniofacial fibrous dysplasia
- mandibular osteotomy
- follow-up studies
- recurrence
- GTP-binding proteins

Introduction

Fibrous dysplasia (FD) is an uncommon skeletal condition in which a normal bone is replaced by fibrotic tissue, resulting in deformity, fractures, pain, and functional impairment.[1] First reported by Lichtenstein in 1938,[2] the disease is classified in two large groups: monostotic (70%) and polyostotic (30%).[3] Clinical onset of the pathology is often observed during childhood or puberty, with a slow progression that continues into adulthood.[4] The etiology of FD is related to a

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mutation in *GNAS* gene (20q13) resulting in the overexpression of cAMP reactive units and increased cell proliferation with inadequate differentiation and disorganized fibrotic bone matrix.[5]

The craniofacial skeleton may be affected in up to 25% of monostotic cases and is involved in almost 90% of patients with the polyostotic form.[6] Clinical presentation in this anatomical area may be variable depending upon the afflicted bones or the structures adjacent to them. Common complaints include facial asymmetry, optic nerve compression, nasal obstruction, malocclusion and obstruction of the auditory canal.[7,8]

Care of patients afflicted with craniofacial fibrous dysplasia (CFD) is complex due to its functional and aesthetic impact as well as the risk for recurrence. The ongoing debate includes the ideal surgical techniques for its management and timing for surgery.[1,9] Evidence-based care for this pathology is scarce because the literature is largely limited to case series or case reports; additionally no information is available from Latin American countries or other developing nations.

The objective of this work is to present our institution's experience in the characterization, evaluation, and management of CFD to better understand its clinical manifestations and help integrate surgical protocols.

Patients and Methods

We conducted a retrospective study that included all individuals with CFD who presented to the craniofacial surgery clinic from January 2012 to December 2019. Both newly referred and follow-up patients were included in the series.

The diagnosis was based on clinical evaluation and imaging findings. Data were obtained from each patient's medical record and entered into a datasheet that included demographic characteristics, clinical presentation, date of disease onset, afflicted bones, radiological studies, quantity and type of surgeries performed, recurrence (considered positive when showing bone growth clinically or on radiological studies), and complications.

Descriptive analysis of the demographic and clinical characteristics of the patients was performed. Mann–Whitney *U* test was performed to evaluate recurrence-free years between en bloc resection and bone burring. Pearson's chi squared test was performed to evaluate association between the type of surgery and recurrence as well as type of disease and recurrence. Full approval by the institutional ethics board was received (registration number 05–65–2020).

Results

Eighteen patients were included in the study, 11 females (61%) and 7 males (38%). The median age was 10.5 years (range: 1 to 38). The most commonly affected age group was that of patients under 12 years old (9 patients, 50%).

Clinical Presentation

Aesthetic nonconformity was the main cause for consultation (17 patients, 94%). Accompanying clinical manifestations included headaches in two patients (11%), airway obstruction due to mass effect in three cases (17%), and visual impairment secondary to compressive optic neuropathy in three patients (17%). One patient presented *Café au Lait* spots associated with McCune–Albright syndrome. The mean time from diagnosis to referral to the clinic was 3 ± 2.1 years.

Radiological and Biological Evaluation

All patients underwent complete skull CT scans with three-dimensional (3D) reconstruction. Disease was classified as monostotic in 4 patients (22.2%) and polyostotic in 14 (77.7%), with a total of 50 bones exhibiting signs of FD. The zygoma, frontal, and maxillary bones were the most commonly affected bones with eight cases each (16%), followed by the mandible and orbit with six cases each (12%). The remainder of the structures involved were the ethmoid, the nasal bones, temporal and parietal bones, and the cranial base. Three patients had extracranial disease affecting the femur.

Bilateral presentation was seen in 8 patients (44%), while 10 patients showed unilateral presentation (6 right and 4 left) (►**Tables 1** and **2**).

Histopathological analysis was performed in all patients and the diagnosis was confirmed as fibrous dysplasia. No *GNAS* mutation test was performed.

Surgical Treatment

A total of 84 surgeries were registered, resulting in an average of 4.6 ± 3.7 procedures per patient. The most common intervention was bone burring with 36 procedures (42.8%), followed by 15 cases of en bloc resection (17.8%) (►**Figs. 1**–**3**). The remainder of the surgeries were done for reconstructive or camouflage purposes. One hemi-mandibulectomy and two maxillectomies were performed and reconstructed with osteocutaneous free flaps. No patient received bisphosphonates or corticosteroids.

The mean follow-up time after first surgery in our institution was 12.1 ± 8.1 years. Twenty-six episodes of recurrence were identified in 10 patients. Five cases were seen after en bloc resection (19.2%), and 21 (80.8%) were identified in the bone burring group ($p = 0.09$ odds ratio [OR]: 0.6, confidence interval [CI]: 95%: 0.31–1.18). Two recurrences occurred in the monostotic group and 24 in the polyostotic group ($p = 0.19$; OR: 3.17; CI 95%: 0.51–19.6).

Bone burring had an average of 13.6 recurrence-free years and en bloc resection of 15 years, there was no statistical significance regarding one treatment against the other ($p > 0.5$).

Posttreatment complications include limitation of eye movements in one patient, chronic pain in another one, and malocclusion in two cases. No malignant transformation was identified in any case.

Discussion

Fibrous dysplasia is a rare pathology representing 5 to 7% of all benign bone tumors. It is estimated to affect one in 30,000 people, but its true prevalence remains difficult to estimate

Table 1 Demographic characteristics, clinical features, and surgical management of the patient population

Patient	Age at first surgery (years)	Gender	Type of involvement	Affected bones	Number of surgeries	Clinical findings	Main surgical procedures	Complications
1	8	Female	Polyostotic	Femur, frontal, ethmoid, nasal, skull base	7	Aesthetic nonconformity airway obstruction	Resection of tumor and Hip Replacement, burring (3), pericranial flap, lipoinjection	Nasal obstruction
2	29	Female	Polyostotic	Temporal, parietal	1	Headache, aesthetic nonconformity	Burring	–
3	9	Female	Polyostotic	Frontal, maxilla, malar, temporal, ethmoid, skull base	10	Aesthetic nonconformity, Hemianopsia Malocclusion Angle C, Facial deformity	Intracranial tumor resection (2) Left hemimaxillectomy Peroneus flap. Frontal flap	Loss of orbital integrity. Optic nerve atrophy
4	25	Male	Monostotic	Mandible	3	Aesthetic nonconformity, Pain, Malocclusion	Left hemimandibulectomy Peroneus flap.	Dental loss, malocclusion.
5	6	Male	Polyostotic	Frontal, Maxilla, mandible, femur	7	Aesthetic nonconformity, Facial deformity, Airway obstruction	Burring (5), Tumor resection Femur Elongation	–
6	38	Male	Polyostotic	Malar, maxilla	5	Aesthetic nonconformity, Malclusion facial deformity	Maxillectomy Peroneus flap. Lower eyelid reconstruction, canthopexy	Dental loss, malocclusion.
7	16	Male	Monostotic	Malar	1	Aesthetic nonconformity, Facial deformity	Burring	–
8	1	Female	Polyostotic	Frontal, maxilla, orbit, malar, mandible	3	Aesthetic nonconformity, facial deformity, airway obstruction	Burring (2) Tracheostomy	Repeated airway infections
9	18	Female	Polyostotic	Frontal, malar	10	Facial deformity	Lipoinjection (3) Frontal abscess drain Burring	Frontal abscess formation
10	4	Female	Polyostotic	Maxilla, orbit femur	1	Aesthetic nonconformity, facial deformity, varus deformity of lower limb Stains café au lait, McCune–Albright syndrome	Burring, Referred to endocrinologist	Chronic pain

Table 1 (*Continued*)

Patient	Age at first surgery (years)	Gender	Type of involvement	Affected bones	Number of surgeries	Clinical findings	Main surgical procedures	Complications
11	8	Male	Polyostotic	Maxilla, Mandible, orbit, frontal	5	Aesthetic nonconformity, facial deformity, dental crowding, orbital compression, recurrent airway infections	Burring (3) Frontal craniotomy with tumor resection and frontal titanium plate placement	–
12	7	Male	Polyostotic	Maxilla, orbit	14	Aesthetic nonconformity, facial deformity, ptosis	Resection (2) Cranial burring (12)	–
13	17	Male	Polyostotic	Maxilla, Malar, orbit	1	Aesthetic nonconformity, facial deformity, eye movement limitation	Burring	Eye movement limitation
14	15	Female	Monostotic	Mandible	2	Aesthetic nonconformity, facial deformity	Burring Tumor resection	–
15	12	Female	Polyostotic	Frontal, ethmoid	6	Aesthetic nonconformity, Facial deformity, Strabismus.	Strabismus correction, cranial reconstruction, tumor resection, nasal reconstruction, anterolateral thigh flap	–
16	23	Female	Polyostotic	Mandible, orbit, Malar	4	Aesthetic nonconformity, facial deformity, exophthalmos malocclusion angle C	Burring (3) Tumor resection	–
17	7	Male	Monostotic	Malar	2	Aesthetic nonconformity, facial deformity.	Tumor resection Burring	–
18	10	Female	Polyostotic	Frontal, nasal, ethmoid	2	Cantal dystopia	Tumor resection Burring	–

Table 2 Overall view of the afflicted bones

Involved bones	Number of affected bones
Maxilla	8 (16%)
Malar	8 (16%)
Frontal	8 (16%)
Mandible	6 (12%)
Orbit	6 (12%)
Ethmoid	4 (8%)
Nasal	2 (4%)
Skull base	2 (4%)
Temporal	2 (4%)
Parietal	1 (2.2%)

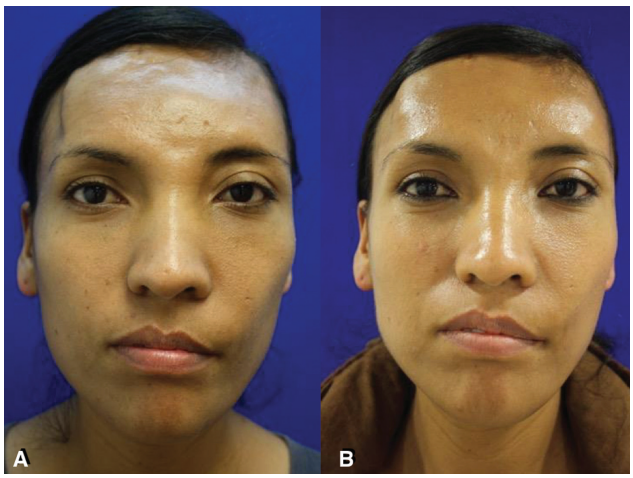

Fig. 1 (**A**) Pre and (**B**) postoperative images of a 30-year-old female patient with frontal bone CFD.

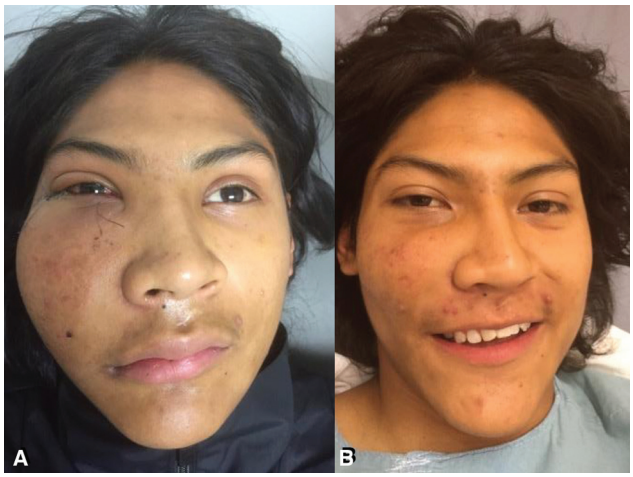

Fig. 2 (**A**) Pre and (**B**) postoperative images of a 17-year-old male patient with zygomaticomaxillary complex CFD.

due to the unknown frequency of asymptomatic lesions.[4] CFD is a form of the disease in which the main involvement occurs in the bones of the craniofacial skeleton. Between 50 and 100% of patients with polyostotic disease will have craniofacial involvement, while only 10 to 25% of monostotic disease will affect craniofacial structures[10]

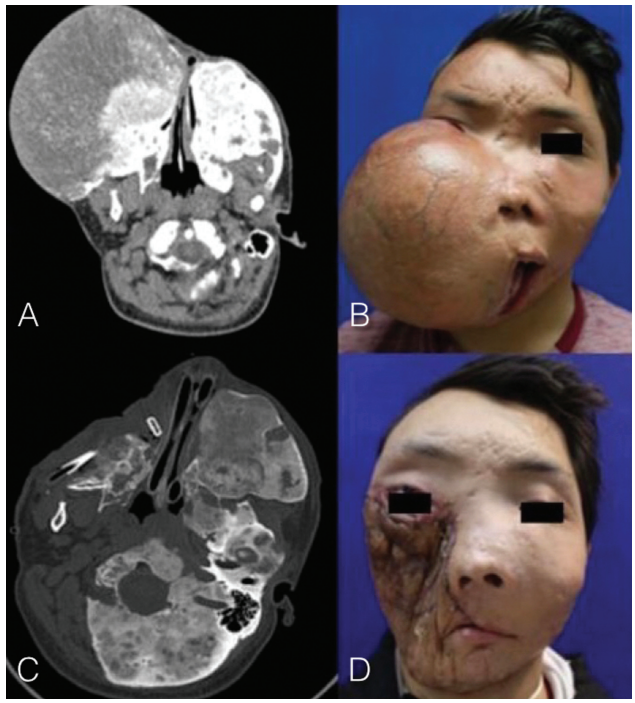

Fig. 3 (**A** and **B**) Pre and (**C** and **D**) postoperative images of a 17-year-old male patient with polyostotic CFD involving the zygomaticomaxillary complexes and orbits.

Successful clinical management of patients with CFD is complex due to the aesthetic and functional alterations caused by the disease, its chronicity, and the need for long-term care.[8] Therefore, intervention by a multidisciplinary team is important. Surgery is the mainstay of treatment in CFD, but the ideal techniques, timing, and indications are still debated.[1]

Large systematic reviews such as those by Wu[11] and Yang[12] provided us a comprehensive view of the clinical manifestations of the disease. As a matter of fact clinical presentation in our patients is similar to their descriptions. For example, the zygomaticomaxillary complex was the most commonly affected structure and most patients had unilateral presentation in our population. However, some differences arose in our series, such as the polyostotic form being dominant (77.7%) and having a higher prevalence of female patients. Differences may be attributed to the small sample size and selection bias due to our institution being a national referral center.

To this day, no evidence-based guidelines have been established for the surgical management of CFD. The literature is largely limited to single-institution case series, group consensus or narrative reviews.[13,14] The broad clinical spectrum of the disease further complicates decision-making, leading surgical teams to individualize treatment in most cases. Regardless of the elected procedure reconstructive goals should focus in the prevention of functional loss, reduction of physical disfigurement, prevention of secondary deformity, and minimization of long-term morbidity.[13]

Bone burring achieves volume reduction and allows for smooth bone contouring. It was the most commonly

performed procedure in our series, mainly due to the high prevalence of polyostotic disease. The procedure may be technically simple but requires finesse to avoid under or over-resection, and damage to adjacent structures.[1]

En-bloc bone resection was reserved for cases with monostotic disease, severe malocclusion or severe airway or oral compromise. Bony reconstruction was successfully achieved with fibula flaps in three cases.

Regrowth is a latent risk for every patient and in some cases may be unpredictable. A notably higher recurrence rate was seen in the bone burring group when compared with en bloc resection (80.8 vs. 19.2%). Even though results did not achieve statistical significance our results coincide with those from Boyce,[7] Gabbay,[15] and Valentini,[16] who report that debulking procedures have a statistically higher risk for recurrence. Sample size and the greater number of patients with polyostotic disease in our series may explain our findings.

En-bloc resection of afflicted bone tissue appears to be the ideal surgical approach for CFD owing to its lower recurrence rate; unfortunately, it is not always feasible or practical. At our institution, resection is reserved for patients with monostotic disease or aggressive bone growth that leads to vision loss or airway/oral obstruction. Bone contouring remains the most popular procedure due to our high prevalence of polyostotic disease, and is also used to manage small contour defects.

Risk of recurrence and the need for secondary procedures should always be explained to patients prior to surgery, especially in cases that will submit to debulking, this can help manage expectations and trace a long-term treatment plan.

Camouflage procedures are also an important tool in the surgical armamentarium for CFD. Lipofilling is especially useful to achieve smoother contours and symmetry.[17] Although not seen in our series, orthognathic surgery with bone debulking may be indicated in patients with mild-to-moderate malocclusion.[18]

Sadly, there are currently no medical therapies capable of altering the disease course in CFD. Bisphosphonates may be effective in treating bone pain but are unlikely to impact the bone's quality or lesion expansion.[19]

The main limitation of this study is its retrospective nature and the small number of patients, which generates difficulty for a solid methodological analysis of the groups. As a strength, it can be mentioned that it is the first and largest Latin American study of this nature.

Conclusion

CFD is a complex pathology that requires an early diagnosis based on clinical, radiological, and histopathological findings. Surgery continues to be the cornerstone of its treatment. Bone burring carries an increased risk for disease recurrence but remains the treatment of choice for polyostotic disease. An individualized approach should be tailored according to the anatomical location of the disease, type of FD, behavior of the lesion, and accompanying clinical complaints.

Ethical Statement

This study was approved by our institutional ethics committee.

Conflict of Interest

None declared.

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